

CHAPTER 15

DRUGS AND GASTROINTESTINAL (GI) DISORDERS

"EVEN THE UGLIEST HUMAN EXTERIORS MAY CONTAIN THE MOST BEAUTIFUL VISCERA."

German saying

SECTION I: INTRODUCTION

The gastrointestinal tract is responsible for the absorption of nutrients and water into the body as well as the elimination of body waste. This system is divided into upper and lower portions.

UPPER GI STRUCTURES

ESOPHAGUS

The esophagus is a long narrow tube that connects the mouth to the stomach. Its function is to deliver materials to their gastric destination. Food and other substances are conducted through the esophagus by a progressive wave of alternating muscle contractions and relaxations and finally deposited into the stomach.

STOMACH

The stomach serves as a holding chamber for food. It includes specialized glands that secrete hydrochloric acid and enzymes to break down foods and prepare them to be absorbed into the body. These gastric chemicals are very caustic and sometimes can actually cause damage to the lining of the gastrointestinal tract (e.g., cause ulcers). Slow, sustained contractions of muscles in the stomach's wall empty the gastric contents into the small intestine.

SMALL INTESTINE

The small intestine is comprised of a long convoluted tube that is divided into the **duodenum**, **jejunum**, and **ileum**. Its functions consist of absorption of nutrients and water as well as retention and passage of waste materials. The movement of intestinal contents is dependent on the contraction of muscle fibers that are located throughout the intestinal wall.

LOWER GI STRUCTURES

These structures comprise the large intestine, and include the **cecum**, **colon**, and **rectum**. The large intestine has two primary functions: absorption and storage. The final, semisolid substances, which result at the end of the large intestine, are called **feces** and remain stored in the colon until expelled through the anal opening during **defecation**. The feces normally consist of 75% water and 25% solid materials (i.e., unabsorbed food, bacteria, and cell debris); however, abnormal functioning of the gastrointestinal tract can cause feces that contain excess water (diarrhea) or are excessively dry and hard (constipation).

GI FUNCTION

Factors that are critical to the proper functioning of the GI system include:

- normal secretions of hydrochloric acid and digestive chemicals by gastric glands
 - adequate protection of the stomach and intestinal lining from caustic digestive enzymes and strong acidic environment
- proper movement of substances (via muscle contractions) through the GI tract
- proper passage of nutrients and water through the GI walls into the body

Interference with these functions can result in GI disorders such as nausea, indigestion, ulcers, diarrhea, constipation, and malnutrition. Some of these GI problems are discussed in the following sections.

SECTION II: ANTACIDS AND H-2 BLOCKERS/ TREATMENTS OF INDIGESTION AND ULCERS

"PART OF THE SECRET OF LIFE IS TO EAT WHAT YOU LIKE AND LET THE FOOD FIGHT IT OUT INSIDE"

Mark Twain

INTRODUCTION

Discomforts of the upper GI tract are often described by the general term **indigestion** and can be associated with many different conditions. Some of these GI disorders are related to eating habits, self-limiting, and respond to symptomatic relief with acid neutralization by OTC antacids. On the other hand, indigestion also can result from severe GI diseases that are life-threatening and require a physician's care. It is essential that the individual determine the cause of the problem.

The following are brief descriptions of conditions that cause gastric distress.

ACUTE GASTRIC IRRITATION

Acute gastric irritation is rapid in onset and generally results from excessive gastric acids associated with overeating, the consumption of spicy or disagreeable foods, overindulgence of alcohol, and extreme emotions. Only indigestion. If any of the following symptoms are associated with the acute gastric irritation, professional assistance should be sought:

- persistent complaints
- extreme nausea or vomiting
- bleeding in stools or vomit
- sharp pains, cramps, or burning sensation

GASTROINTESTINAL REFLUX

The symptoms associated with gastrointestinal (esophageal) reflux are often described by the sufferer as *heartburn* or *sour stomach*. This results from the backflow of stomach contents into the esophagus. The discomfort is associated with the irritation caused by the gastric enzymes and acid on the esophageal wall. The exact reasons for this condition are varied but it is occasionally associated with cancer.

GASTRITIS

The term gastritis refers to inflammation of the stomach lining. This condition can be caused by the chronic consumption of irritating substances such as alcohol or aspirin.

In addition, it might be associated with infections or stress. Bleeding often accompanies this disorder.

ULCERS

Ulcers are erosions (lesions) in the lining of the stomach (approximately 600,000 cases each year in this country) or in the wall of the duodenum of the small intestine (approximately 2.4 million cases per year). Previously, it was thought that stress, diet (especially spicy foods) and excessive gastric secretions caused ulcers. However, because of one of the most impressive recent advances in medicine, we now know that bacteria called *H. pylori* are involved in causing most peptic ulcer disease. Although other factors such as heredity, smoking and stress can contribute, apparently few people get ulcers without being infected by this bacteria. *H. pylori* burrow into the gastric lining and cause a chronic inflammation that makes the stomach or intestine wall vulnerable to erosion. Everyone who is infected with *H. pylori* does not get ulcers; in fact, only 10% to 20% will develop this problem. For those infected who do become ulcer-positive, elimination of the bacteria by antibiotic treatment almost always eliminates the gastric sores.

Little is known about how *H. pylori* is transmitted. Children appear to be more infectious than adults when they have the bacteria. Studies suggest that approximately 50% of the U.S. population is currently infected with *H. pylori*. Because of the relatively low rate of ulcer expression even in those who are *H. pylori* positive, treatment is usually not recommended unless symptoms of ulcers develop.

Approximately 5-10% of the gastric ulcers are associated with stomach cancer. In severe cases extreme bleeding, perforation of the wall of the stomach or small intestine can occur.

THERAPEUTIC APPROACH FOR INDIGESTION

Because of the potentially serious nature of some conditions that cause **indigestion**, the sufferer of gastric discomfort must be certain that self-medication is appropriate; if so determined, several therapeutic approaches can be used to alleviate the problem.

NONMEDICINAL APPROACH

Minimize acid rebound: The stomach will pump out increased amounts of acid and juices following the consumption of all foods and drinks (that includes bland foods and milk products). This causes increased gastric irritation 1-3 hours after eating or drinking; thus, midnight snacks will result in early morning stomach discomfort.

Because the amount of **acid rebound** is directly related to the quantity of food consumed, it is better to eat several small meals than to consume a single large meal each day, if acid rebound is a persistent problem. In addition, the eating of small multiple meals throughout the day maintains constant amounts of food and liquids in

the stomach that help to dilute the strength of the irritating gastric secretions.

Avoid substances that stimulate gastric secretions: Certain substances tend to increase gastric secretions and cause irritations; these include:

cigarettes

caffeine

alcohol

spicy
foods

Avoid emotional situations that enhance gastric activity: Individuals who are unable to cope with stress often suffer ulcers. These people need to learn to handle anxiety and pressure in a less destructive manner.

MEDICINAL APPROACH

Medication for the treatment of indigestion comes in a variety of forms depending on the cause of the gastric irritation. The primary agents used for self-medication are classified as **antacids**. According to FDA guidelines, these products may be promoted for an upset stomach caused by:

- heartburn
- sour stomach
- acid indigestion

OTC products containing these ingredients are frequently used by the public and account for annual sales approaching \$1 billion (the fourth largest OTC category).

All antacids are relatively safe if used by healthy people but regular daily use can cause problems or mask a serious medical condition; for example, antacids might be used to treat what is thought to be heartburn but is actually a heart attack. Taken regularly some antacids can cause bowel irregularities (constipation or diarrhea), mask a peptic ulcer, aggravate a kidney disorder or other problems.

OTC ANTACID INGREDIENTS

Antacids reduce gastric irritation by neutralizing gastric juices. These agents are included in over 500 different OTC products. Besides being useful in the treatment of acute, minor upset stomachs, antacids might also be helpful in the treatment of some forms of ulcer and GI bleeding; however, users of these OTC

preparations for serious medical conditions require the guidance of a physician. In addition, because of their ability to alter the gastric and intestinal environment, it is not surprising that the antacids can alter the absorption of some drugs from the gut. Consequently, as a rule, persons receiving pharmacotherapy should not administer antacid products jointly with their regular medications without consulting their physicians. In fact, antacid products are required to include the following statement:

Antacids may interact with certain prescription drugs. If you are presently taking a prescription drug, do not take this product without checking with your physician.

At least one of the following active compounds is included in almost all antacid products:

Sodium Bicarbonate is the active ingredient found in ordinary *baking soda* and is a potent, effective, and fast-acting antacid. It quickly reacts with the hydrochloric acid of the stomach to form water, sodium chloride, and the gas, carbon dioxide. Although occasional, short-term use is well tolerated, chronic, continual use of this agent can be dangerous and should be avoided. Because of the potential problems with this antacid, its use is rarely recommended by physicians. Some of the adverse actions of sodium bicarbonate include:

Systemic alkalosis: Because bicarbonate quickly enters the blood stream, large doses can alter the normal acid/base balance that exists in the body as well as adversely affect the other aspects of the blood chemistry.

Acid rebound: Increased output of gastric acid, that occurs several hours following the administration of sodium bicarbonate, can leave the user even more uncomfortable than the condition for which the antacid is being used.

Aggravation of high blood pressure: Sodium has been implicated as a factor in high blood pressure; thus, hypertension might be aggravated in patients who consume products with high sodium content (e.g., sodium bicarbonate).

Gas-related discomfort: The formation of carbon dioxide gas from the interaction of sodium bicarbonate and hydrochloric acid causes distension of the stomach resulting in a bloated feeling, belching, and flatulence. In severe overdosing, this distension can lead to perforation of the gut and even death.

Interaction with milk: If sodium bicarbonate is used with milk for an extended period of time a disease called the **milk-alkali syndrome** can result. Symptoms associated with this malady include nausea, vomiting, headache, mental confusion, and constipation. This combination can also lead to the formation of kidney stones.

Calcium Carbonate is also a fast-acting and potent antacid. Compared to sodium bicarbonate, its actions are more prolonged and its side effects less severe. Even though calcium carbonate can be used safely in small doses (0.5 gm) for occasional gastric upset, it should not be used chronically for long-term treatments. Some of the potential adverse actions of calcium carbonate are:

Acid rebound: probably less than sodium bicarbonate (see above).

Hypercalcemia: elevated levels of calcium in the blood that can lead to formation of kidney stones and kidney damage.

Systemic alkalosis: not as much of a problem as with sodium bicarbonate because this compound is less likely to get into the blood.

Milk-alkali syndrome: much more of a problem with sodium bicarbonate use.

Constipation: at one time constipation was considered to be a limiting side effect of calcium carbonate use; however, recent evidence suggests that this is not as much a problem as once thought.

Because of the role of calcium in osteoporosis (extreme loss of calcium from the bones), OTC antacid products have been promoted for use in the treatment of this degenerative process. The rationale is that replacement therapy with calcium carbonate-containing antacids retards the pathogenic loss of calcium from bones that occurs during this disease. The preservation of the calcium in bones helps to prevent stress fractures and other hard tissue injuries associated with osteoporosis. While the benefits of calcium supplementation in the treatment of this disease are well established, the suitability of antacids as a calcium supplement is controversial. As antacids are highly alkaline, there is concern that chronic daily use of these products can cause shifts in the acid/base balance of the body resulting in dangerous metabolic disorders. Consequently, most experts recommend that forms of calcium other than that found in antacids (such as that found in calcium gluconate) be used as dietary supplements to prevent osteoporosis.

Magnesium salts (hydroxide, oxide, carbonate and trisilicate) have less antacid potency than sodium bicarbonate and calcium carbonate. Even so, the magnesium salts are effective acid neutralizers. The actions of these salts are somewhat slow to develop, but are long-lasting. Use of the magnesium compounds is relatively safe even if continued for long periods of time. These agents do not cause the same severe adverse

effects associated with sodium bicarbonate or calcium carbonate use. Because of these factors, magnesium salts are the most commonly used of the antacid ingredients. The administration of magnesium may induce diarrhea, in fact in higher doses it is sometimes used as a laxative. Magnesium has been known to cause CNS symptoms in some people and should be avoided by patients with renal damage. Because of the tendency to promote diarrhea, and have a slow onset of action, magnesium salts are usually combined with aluminum hydroxide or calcium carbonate.

Aluminum salts (hydroxide, carbonate, phosphate) possess the least amount of neutralizing capability of the antacid ingredients, particularly the aluminum phosphate salt, and are almost always combined with a magnesium salt. They are also slower to act than sodium bicarbonate and calcium carbonate. Although aluminum hydroxide is relatively safe, reports of aluminum accumulation after long-term use suggest that prolonged, indiscriminate use of aluminum-containing antacids carry some risk. As with magnesium salts, aluminum hydroxide should not be used by patients with kidney damage. The most common side effect associated with aluminum hydroxide use is constipation.

NONANTACID INGREDIENTS

Alginic acid

This agent is often included in products that contain sodium bicarbonate. Alginic acid helps to form a viscous barrier that floats on the gastric contents and helps to prevent reflux esophagitis (heartburn) by protecting the esophageal lining from the irritation of acidic contents.

Simethicone

Simethicone is classified as an **antiflatulent** due to its ability to facilitate elimination of gas bubbles. Simethicone reduces the surface tension of the gastric bubbles and causes them to either burst or coalesce and be eliminated more easily. This helps to prevent regurgitation of gastric contents into the esophagus (known as esophageal reflux). The FDA has found simethicone to be both safe and effective as an antiflatulent.

ANTACID FORMULATIONS

Antacid products come in an array of different forms: gum, lozenges, tablets, powders, and effervescing liquids. The effectiveness of these products is dependent on their forms and their ability to dissolve and neutralize the acidic environment. For example, as a general rule *liquid suspensions* of antacids have a greater acid neutralizing capacity and more prompt action than comparable chewable antacid tablets.

It is also noteworthy that most OTC antacid products are mixtures of two or more ingredients. The rationales for these mixtures are:

- to combine fast and slow-reacting compounds to give a relatively even, sustained action
- to lower the dose of each component
- to offset annoying side effects

COMMON NONPRESCRIPTION ANTACIDS

Sodium Calcium

Product Bicarbonate Carbonate Magnesium Aluminum Other

Alka-Seltzer

Effervescent Tablets 1700 mg aspirin

Amitone Chewable 350 mg

Amphojel (tablets) 300-600 mg

Chooz (gum) 500 mg

Gaviscon-2 (tablet) 140 mg 40 mg 160 mg alginic acid

Maalox Suspension 45 mg/ml 40 mg/ml

Mylanta (gelcap) 311 mg 232 mg

Phillips Milk of

Magnesia (suspension) 80 mg/ml

Riopan Plus (suspension) Magaldrate

Simethicone

Roloids (tablet) 550 mg 110 mg

Tums Anti-Gas/Antacid (tablets) 500 mg Simethicone

Tums Extra Strength (tablets) 750 mg

Tums Ultra (tablets) 1000 mg

TREATMENT OF ULCERS

Because of the potentially serious consequences of ulcers, the sufferers of these GI erosions should not attempt to self-medicate their problem without first receiving professional advice. Until recently, ulcers were typically treated with antacids (to reduce the irritation of gastric acids) and special antihistamines known as H-2 blockers (e.g., **Tagamet**, **Zantac**, and **Pepcid**). Although these drugs are still useful in the treatment of some types of ulcers, and heartburn, the discovery that the bacteria *H. pylori* causes the majority of ulcers has dramatically altered the therapeutic approach. Use of antacids and H-2 blockers reduce gastric irritation and help to accelerate ulcer healing, but in more than 90% of these patients the ulcers recur. Thus, treatment with these drugs is not a cure, but only helps the disease go into remission. In contrast, treatment with antibiotics (e.g., combinations of tetracycline, metronidazole and a bismuth salt) to eliminate the *H. pylori* infection has a cure rate of almost 90%. Undoubtedly, this new approach will have a dramatic impact on future ulcer therapeutics.

H-2 BLOCKERS

These agents are classified as antihistamines, but have pharmacological effects much different than those drugs of the traditional antihistamine family. The H-2 blockers used to include some of the most frequently prescribed drugs in the world and include **Tagamet** (cimetidine), **Zantac** (ranitidine), and **Pepcid** (famotidine) and act by blocking gastric secretions. As mentioned above, the H-2 blockers have been the mainstay in ulcer therapy for more than 20 years. However, because of the discovery of the association between *H. pylori* and ulcers, the future of the H-2 blockers in the treatment of ulcers is being questioned. Some have suggested that these drugs will continue to be useful in ulcer treatment, especially because 10% of the ulcer patients are not infected with *H. pylori* bacteria.

Another common use for the H-2 blockers is the treatment of esophageal reflux (heart burn). This discomfort is caused by the regurgitation of gastric juices onto the sensitive

esophageal lining and is experienced regularly by over 60 million Americans. Because the H-2 blockers reduce gastric secretions, the drugs provide significant relief from this common complaint. In fact, this gastric problem is so common that the FDA authorized a low dose form of Tagamet (**Tagamet HB**), Pepcid (**Pepcid AC**), Zantac (**Zantac-75**), and nizatidine (**Axid AR**) to be sold as an OTC heartburn remedy. The antacids are also commonly used to relieve the discomfort associated with esophageal reflux. These agents are often effective initially, but their benefits are typically short-lived and usually minimal in moderate to severe episodes.

SECTION III: LAXATIVES-TREATMENT OF CONSTIPATION

"ONE IS NOT ALTOGETHER FIT FOR THE BATTLE OF LIFE WHO IS IN PERPETUAL CONTENTION WITH HIS DINNER"

Meredith

INTRODUCTION

Manufacturers of laxatives have been very successful in persuading the public that *bowel regularity* is necessary for a normal, vigorous life while constipation is the root of many medical ills. Consequently, the demand for laxative products recently has increased dramatically and currently accounts for almost 500 million dollars annual sales in the United States.

Most laxatives act by increasing the amount of water in the stools; this softens the stool mass and facilitates the movement of bowel contents through the intestines. The most common reason given for the consumption of laxatives is to establish **regularity**. It should be understood that regularity of bowel movements varies considerably between individuals and is not essential for health. There is no evidence to support the theory that a daily bowel movement is vital to one's medical well-being. In fact, most authorities claim that anything between 3 movements per day to 3 per week is normal. Another misconception is that some laxatives are *natural* medicines. There is nothing natural about taking a drug to make you defecate.

Because of these misunderstandings about bowel function, laxatives are extensively misused especially by the elderly. **There are few legitimate reasons for taking a laxative** since most constipation problems can be resolved by increasing the fiber content of the diet, increasing exercise, and increasing fluid intake. If a laxative is indicated, it should not be used for longer than one week. Many instances of individuals developing a **laxative habit** have been reported. This results from overuse of the agents and

is encouraged by a rebound constipation that occurs when long-term laxative treatment is discontinued.

CONSTIPATION

Constipation generally means decreased elimination of fecal material and is often associated with the difficult passage of dry, hard stools that are dehydrated due to their prolonged presence in the colon. Because of tremendous individual variation in bowel habits, the frequency of bowel movements is not as good an indication of constipation as the consistency of the stools. Other symptoms that might accompany constipation problems include:

- lower abdominal pressure**
- low back pain**
- lack of appetite**
- headache**

The causes of legitimate constipation are varied and include:

- inflamed colon (colitis)**
 - decreased contraction of intestinal muscle**
(causes retarded passage of intestinal substances)
- overuse of laxatives**
- drugs (i.e., some antacids, anticholinergic drugs, or narcotics like codeine)**
- cancer and other obstructions of the bowel**
- changes in diet**

Constipation due to pathology (disease) should not be self-treated with an OTC laxative. Such an approach can aggravate the problem and might be dangerous. It is also important to note that **no laxatives should be used if cramps, colic, nausea, vomiting, or other symptoms of appendicitis or**

any undiagnosed abdominal pain is present. If one is certain that the cause of the constipation is nonorganic (i.e., not due to disease), perhaps a laxative might be justified for a short period of time. There are three general mechanisms of laxative action. **First**, laxatives can change the nature of the composition of the stools and cause retention of fluid, thereby increasing their mass and softness. **Second**, laxatives can act directly on the lining of the colon and decrease the absorption of water from the stool material. **Third**, laxatives can increase the muscular activity of the intestines and cause stools to pass through more quickly, thus decreasing water absorption.

The following are compounds that are commonly used as laxatives.

BULK-FORMING LAXATIVES

These are considered to be the safest type of laxative and can be taken for extended periods of time with little threat of serious side effects. These agents tend to initiate normal physiological mechanisms for evacuating intestinal contents. For this reason, these laxatives are generally used as initial therapy for constipation.

Mechanisms of action: These agents absorb water and cause a softening of stool mass. In addition, the bulk-forming laxatives cause an enlargement of the stools that stimulates propulsive movements in the GI tract and encourages the passage of intestinal contents.

Onset of action: These drugs are usually effective after 12-24 hours and can require as long as 3 days to exert an effect (generally regarded as slow-acting laxatives).

Uses: These drugs are used in the management of simple constipation and help soften stools in patients with painful hemorrhoids.

Adverse effects: These compounds should be taken with large amounts of fluids, otherwise, obstruction of the intestine can occur.

Examples and sources:

Dietary fiber- These can be easily incorporated into the normal diet and, for most people suffering from constipation, should be tried before other laxative approaches. Usual sources of dietary fiber are whole grains, bran, vegetables, and fruit.

Semisynthetic cellulose- These are indigestible derivatives of the compound cellulose and include the agents **methylcellulose** and **carboxycellulose**.

Polyacrylic resins- The compounds in this group include **polycarbophil** and **calcium polycarbophil**. These resins have more water-absorbing ability than do the other bulk-forming compounds.

Others- These work in a manner similar to the afore mentioned agents and include psyllium, kelp, plant gums (karaya), agar, and acacia.

LUBRICANT LAXATIVES

Lubricant drugs differ from other laxatives in that they do not affect bowel movement.

Mechanism of action: The lubricants coat the stools and prevent the absorption of fecal water in the colon; consequently, the stools remain softer, pass more easily, and with greater comfort.

Onset of action: 6-8 hours

Uses: The lubricant laxatives are useful in the treatment of patients who should avoid straining when trying to pass stools (e.g., following abdominal surgery, or removal of hemorrhoids, patients suffering from hernias, hypertension, or heart attacks).

Adverse effects: The oily compounds that comprise this group of laxatives can interfere with the absorption of nutrients, such as vitamins, calcium, phosphates, and even water from the gut and intestines. These agents can also affect the absorption of certain drugs. Because of the adverse effects, use of these agents as laxatives is discouraged.

Example: Mineral oil (often mixed with other laxatives in OTC products).

STIMULANT LAXATIVES

These laxatives are effective and must be used cautiously due to potentially dangerous side effects. Because of their effectiveness these agents are commonly overused and abused. Stimulant laxatives are not recommended for use as the initial treatment for constipation. Administration of these drugs for more than one week is strongly discouraged. The effectiveness of these agents is highly dose-dependent. In addition, the stimulant laxatives do not necessarily assist the body to return to normal bowel function.

Mechanism of action: Stimulant laxatives irritate the intestinal lining which in turn causes an increase in wavelike muscle contractions in the intestinal wall, that enhances the propulsion of intestinal contents.

Onset of action: The laxative effect occurs 6-12 hours following administration.

Uses: Due to their potent laxative properties, the stimulants are used to empty intestines prior to exploratory or surgical procedures on the bowel.

Adverse effects: Due to the irritative properties of the stimulant laxatives, cramping can result from their use. In addition, excessive diarrhea and loss of water resulting in chemical imbalances can occur. Frequent use (2-3 times weekly) has been associated with anatomical changes in the colon. The functional consequences of these changes are unclear. The FDA has recommended the removal of phenolphthalein, a stimulant-type laxative, due to a possible link with cancer. The ability of this drug to

cause cancer has only been established in laboratory animals and the relevance to humans is unclear.

SALINE LAXATIVES

Use of saline laxatives is only recommended in situations when prompt emptying of the bowel is necessary. These are not good laxatives to use for prolonged treatment of constipation.

Mechanism of action: The saline laxatives draw large amounts of water from the body into the intestines, which in turn increases the pressure on the intestinal walls and stimulates the movement of bowel contents.

Onset of action: Laxative effect occurs from 1/2 to 3 hours following administration of the saline laxatives.

Uses: Used to rapidly evacuate the bowels in cases of suspected poisoning or in preparation for intestinal exploration (i.e., endoscopic examination).

Adverse effects: Because these agents can cause significant loss of body water into the bowels, prolonged use can result in dehydration. Other adverse effects can also result from the absorption of cations found in these products such as magnesium and sodium; for example, hypotension (low blood pressure), hypertension (high blood pressure), muscle weakness, heart arrhythmias, and CNS depression have been associated with the use of saline laxatives.

Examples:

magnesium salts (citrate, hydroxide, sulfate)

sodium phosphate

sodium biphosphate

EMOLLIENT LAXATIVES

When administered orally, these laxatives are of little benefit in the treatment of long-term constipation. These agents can enhance the absorption of certain drugs and should not be used by individuals who are taking other medications.

Mechanism of action: These laxatives function like a detergent to facilitate the mixture of fatty and water-soluble substances in the stools; as a result, the fecal mass is softened and passes through the bowels more easily.

Onset of action: 12-72 hours.

Uses: These agents are used to soften hard, uncomfortable feces for short periods of time (up to a week). This is particularly useful for patients who have medical conditions that would be aggravated with strained defecation (e.g., surgical patients, hemorrhoid sufferers, etc.).

Adverse effects: These agents are usually well tolerated but can enhance the passage of undesirable substances through the GI wall into the systemic circulation.

Examples:

dioctyl salts (sodium, calcium, potassium docusate

LAXATIVE MISUSE

Because of the erroneous claims made for laxative products, some individuals become dependent on these substances. The frequent use of laxatives can result in abnormal bowel patterns that convince the user that constipation is a problem. This belief encourages continuation of the laxative and results in drug-dependence. It is important that the potentially serious consequences of such a drug habit be understood. The following conditions can result from laxative abuse:

- **excessive diarrhea** leading to dehydration and chemical imbalances in the body
- **loss of intestinal muscle tone**
- **liver disease**
- **abdominal cramps**
- **inflammation of the intestinal lining**
- **tissue destruction in the colon**

Individuals who use laxatives on a regular basis should be weaned from these agents before permanent damage results.

LAXATIVE PRODUCTS

Product Bulk Lubricants Stimulants Saline Emollients

Citrucel Powder methylcellulose

Citroma magnesium

Colace Liquid docusate

Correctol Caplets bisacodyl

Correctol Herbal Tea senna

Dulcolax bisacodyl

Ex-Lax Stool

Softener docusate

Ex-Lax Gentle

Tablets sennosides

Feen-A-Mint bisacodyl

FiberCon Tablets polycarbophil

Fleet Mineral Oil

Enema mineral oil

Fleet Ready-to-Use

Enema sodium

phosphate

Haleys M-O mineral oil magnesium

Maltsupex Liquid barley malt

Metamucil Fiber psyllium

Milk of Magnesia magnesium

Senokot Tablets senna

SECTION IV: ANTIEMETICS

(DRUGS TO TREAT VOMITING)

"A HUMAN BEING IS AN INGENIOUS ASSEMBLY OF PORTABLE PLUMBING."

Christopher Morley

INTRODUCTION

The vomiting (**emesis**) reflex is a protective mechanism utilized by the body to rid itself of irritating substances and poisons. Vomiting, or associated nausea, can also occur in conjunction with a variety of other conditions such as motion sickness, pregnancy (morning sickness), mild infectious diseases, extreme pain, stomach upset, severe headaches, head injuries, nauseating sensory input (sight, smell, or tastes) and drugs.

The vomiting process consists of complex interactions between the structures of the upper GI tract, the upper respiratory tract, the diaphragm, and the abdominal muscles. This reflex is coordinated by the **vomiting center** of the brain, as follows:

First, the initial symptoms associated with vomiting include a feeling of nausea, sweating, or increased salivation and heart rate.

Second, the vomiting is initiated with a deep breath, closure of the epiglottis (to prevent entry of vomitus into the lungs), and elevation of the soft palate (to prevent entry of vomitus into the nose).

Third, the contents of the stomach are forced up through the esophagus by means of a forceful contraction of the abdominal muscles and the diaphragm. This action compresses the stomach and thrusts the gastric contents up into the mouth.

COMPLICATIONS

Almost everyone has experienced nausea and vomiting. The results, while rather *distasteful*, are usually trivial; however, the possibility of serious consequences does exist. For example:

Excessive vomiting can cause severe loss of water and dehydration with associated chemical

imbalances in the body. This is a particular danger in very young children.

Occasionally, closure of the epiglottis does not occur, permitting the **vomit** to enter the **airways and lungs** causing a very serious medical condition. This problem is often associated with vomiting by an unconscious patient.

Continual, violent vomiting can actually harm the stomach and esophageal linings. The retching forces and caustic gastric juices can seriously damage the tissue walls that line these structures.

SIGNS OF SERIOUS VOMITING

If the following conditions are associated with vomiting, immediate medical care should be sought:

- blood found in the vomitus
- continual vomiting for 2 or 3 days
- stomach pain or cramps associated with the vomiting
- severe retching and/or extremely forceful vomiting
- vomiting in newborn infants not associated with feeding

ANTIEMETIC MEDICATIONS

Several types of antiemetic products are available OTC and by prescription. Selection of an antiemetic depends on the cause and severity of the vomiting.

OTC PRODUCTS

ANTIHISTAMINE-CONTAINING DRUGS

The FDA advisory review panel has found that the nonprescription antiemetics are only useful in the treatment of nausea and vomiting related to **motion sickness**. Because these agents are most effective in the prevention of motion sickness rather than its elimination, the OTC antiemetics should be taken 30-60 minutes prior to traveling. The active ingredients in these products are antihistamines that include:

Cyclizine (Marezine)

- should be taken 30 minutes before travel
- can be used in children 6-12 years of age
- its use in pregnancy is considered to be safe, but ineffective against morning sickness

Meclizine (Bonine, Dramamine II)

- should be taken 1 hour prior to travel
- has a long duration of action (up to 24 hours)
- not recommended for children under 12 years of age

Dimenhydrinate (Calm-X, Dramamine, Triptone)

- can use in children 2-5 years old
- administer 30-60 minutes before departure

The most frequent side effect associated with the use of antihistamine-containing antiemetics is drowsiness. For this reason, driving a car or operating dangerous machinery is not recommended when using these agents.

PHOSPHORATED CARBOHYDRATE (EMETROL)

This product contains sugars (carbohydrates) mixed with phosphoric acid as an antiemetic. Its usefulness is not well documented in spite of the claims by many of its users that it is both effective and safe.

SWEET SYRUPS

Some individuals claim that sweet syrups, such as coca-cola syrup, mixed with crushed ices affords some antiemetic relief.

PRESCRIPTION DRUGS

PHENOTHIAZINES OR TRANQUILIZERS (THORAZINE, COMPAZINE, TORECAN)

These agents are considered most effective in the treatment of vomiting caused by gastrointestinal disorders (e.g., flu or other viral infections) or drugs. The

phenothiazines are generally not used to treat motion sickness.

ANTICHOLINERGIC DRUGS (SCOPOLAMINE)

Scopolamine is effective in the prevention of motion sickness, however, systemic use can cause significant side effects. A transdermal delivery system for scopolamine has been made available which prevents motion sickness with minimal anticholinergic side effects (see **Chapter 4**). The product is called **Transderm-scop** and consists of a circular flat plastic disc containing scopolamine that is placed behind the ear. The scopolamine passes through the skin and results in low, sustained blood levels of the drug. This product should not be used by children.

ANTI-HISTAMINES

Some prescription antihistamines, that are commonly used to treat nausea and vomiting, include:

diphenhydramine (Benadryl)

meclizine (Antivert)

hydroxyzine (Atarax)

Another antihistamine, **Doxylamine (Bendectin)** also was frequently used to treat nausea associated with *morning sickness* during pregnancy. However, Merrell-National Laboratories withdrew this product from the market due to a lawsuit which claimed use of this compound caused congenital defects in offspring. Incidentally, the suit was unsuccessful, but Merrell-National Laboratories feared that in the future, costly suits would likely be filed against Bendectin, so this company persisted in its decision to discontinue production of this product.

SECTION V : ANTIDIARRHEALS

INTRODUCTION

Diarrhea is characterized by the frequent passage of loose and watery stools. The frequency of bowel movements is not the critical factor in diagnosing diarrhea; more important is the excess water in the feces. It should be realized that diarrhea of itself is not a disease but the expression of some underlying medical disorder. Diarrhea can result from a variety of factors such as psychological disorders, neurological diseases, gastrointestinal infections, allergic reactions, inflammation, irritating substances, and changes in diet.

The onset of diarrhea might be abrupt and accompanied by symptoms such as weakness, gas, abdominal cramps, fever, and vomiting. In contrast, chronic diarrhea is characterized by continual passage of loosely formed stools and can be associated with emotional stress, chronic laxative use, or chronic diseases such as diabetes or cancer.

THERAPY

Bear in mind that diarrhea is a symptom and treatment of diarrhea is not a cure for the underlying disorder. Self-medication with OTC antidiarrheals is appropriate only when treating mild, simple, self-limiting diarrhea (e.g., traveler's diarrhea). Over 100 OTC antidiarrheal products are currently available and the FDA requires that the following warning be placed on their labels:

Warning: Do not use for more than 2 days or in the presence of high fever or in infants or children under 3 years of age unless directed by a physician.

NONMEDICINAL TREATMENT

As a rule, mild to moderate diarrhea is self-limiting and the primary concern is the replacement of fluids, important nutrients, and chemicals that have been lost. The following are therapeutic steps that have been suggested as treatment for diarrhea in children over the age of 3 years.

First, allow the GI tract to rest for several hours; i.e., don't give fluids or food to the child (if the fluid loss has been severe, dehydration may be a problem, in which case fluid replacement should be started immediately).

Second, after 4 - 6 hours, start fluid replacement using small amounts of drinks such as:

Decarbonated soda beverages: soda pop that has all the carbonation removed; this can be achieved by stirring the soft drink in an open glass.

Liquid gelatin dessert: Jell-O or Royal gelatin prepared as a liquid with twice the normal amount of water added.

Gatorade

Commercial preparations: e.g., **Pedialyte, Infalyte, or Rehydralyte;** these are preparations available at the pharmacy without a prescription.

If following this treatment the diarrhea persists, then a physician should be consulted.

MEDICINAL TREATMENT

The FDA advisory review panel on antidiarrheal ingredients found that only **opiates** (narcotics) and **polycarbophil** were both safe and effective for nonprescription use. The panel was unable to find evidence to support the effectiveness of other OTC antidiarrheal products.

The following are the drug groups commonly included in antidiarrheal products:

EFFECTIVE ANTIDIARRHEAL AGENTS

Opiates: All opiate agents (e.g., heroin, morphine, codeine) block the activity of the muscles of the small intestine and cause constipation in the normal individual or decrease the passage of watery stools in the patient with diarrhea.

An OTC liquid formulation of the drug, loperamide (brand name, **Imodium A-D**), is also an effective antidiarrheal agent. This drug, previously available only by prescription, is classified as a nonabusing narcotic agent. Loperamide is a fast-acting drug that slows the passage of bowel content causing firmer stools at longer intervals. The OTC product is in liquid form, however, loperamide capsules continue to be available only by prescription. This drug is only to be used for acute, nonspecific diarrhea associated with a self-limiting condition. It should not be used for diarrhea caused by infection because it may delay the expulsion of harmful substances from the bowel. Situations when self medication of OTC loperamide are not recommended are (1) persistence of diarrhea for

greater than 48 hours, (2) diarrhea accompanied by fever over 101° F, (3) blood in the stools, or (4) a history of liver disease.

Paregoric contains small amounts of morphine and effectively relieves diarrhea and associated cramping. Prolonged use can lead to dependency and abuse.

Diphenoxylate has minimal potential for being abused. Sometimes it is combined with an anticholinergic agent (marketed as **Lomotil**-prescription drug); the side effects of a large dose of the anticholinergic drug are very unpleasant and discourage excessive use of this product.

Polycarbophil: This compound is an inert resin that absorbs water in excess of 60 times its weight and is both safe and effective in improving the consistency of stools.

INEFFECTIVE ANTIDIARRHEAL AGENTS

Adsorbents: These agents are found in OTC products more frequently than any of the other antidiarrheal compounds. These drugs nonspecifically adsorb GI contents such as nutrients, gastric secretions, microorganisms, poisons as well as other drugs. Examples of the agents are:

activated charcoal

attapulgit

bismuth compounds

kaolin

pectin

Lactobacillus agents: The use of the bacteria strain, *lactobacillus*, in antidiarrheal preparations is highly controversial. While it is true that

bacteria and other microorganisms inhabit the GI tract and contribute to normal GI function, there is no evidence that stocking the bowels with lactobacillus (a normal inhabitant of the intestines) alters the medical course of the diarrhea sufferer. Examples of products containing this bacteria include:

Pro-bionate

Superdophilus

Yogurt

Bulk-Producing Agents: These agents are supposed to adsorb free fecal water and cause the formation of solid stools. Paradoxically, these agents are also used to soften stools in patients suffering from constipation. The most common example is **carboxymethylcellulose**.

SELECTED ANTIDIARRHEAL PRODUCTS

Products Opiates Adsorbents Other Agents

Donnagel attapulgate

Imodium A-D loperamide

Kaopectate attapulgate

Kao-Paverin Caplets loperamide

Kao-Paverin Liquid pectin, kaolin,

bismuth subsalicylate

Mitrolan Tablets polycarbophil

Pepto-Bismol bismuth subsalicylate